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In re application of:

Avi Ashkenazi, et al.

Application Serial No. 09/904,766

Filed: July 12, 2001

For: **PRO269 POLYPEPTIDES**

) Examiner: Kemmerer, Elizabeth
)
) Art Unit: 1646
)
) Confirmation No. 4054
)
) Attorney's Docket No. 39780-1618P2C33
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DATE MAILED: January 17, 2006

**PETITION FOR DESIGNATION AS NEW GROUNDS OF REJECTION
UNDER 37 C.F.R. §1.181**

MAIL STOP PETITION

Commissioner for Patents

P.O. Box 1450

Alexandria, Virginia 22313-1450

Sir:

This Application is under Appeal. An Examiner's Answer was mailed on November 15, 2005 in this case. This petition is filed:

☒ within two months of the mailing of the Examiner's Answer (January 15 and 16, 2006 being a Sunday and Federal Holiday in the District of Columbia, respectively).

The proposed Reply Brief

☒ has been filed separately;
☐ is attached;
☒ with a request for Oral Hearing; and
☒ a copy of the Petition for designation of new grounds of rejection in the Examiner's Answer under 37 CFR §1.181

The application status is:

01/20/2006 BABRAHA1 00000063 081641 09904766
02 FC:1464 130.00 DA

☐ Small Entity—fee \$
☒ Large Entity—fee \$
☐ Enclosed is Check No. _____ in the amount of \$_____.
☒ The Commissioner is authorized to charge (or credit any overpayment) Deposit Account No. **08-1641** (referencing Attorney's Docket No. **39780-1618P2C33**) in the amount of **\$130.00** for the Petition Fee.

STATEMENT

An Appellants' Appeal Brief was filed on September 13, 2005 and an Examiner's Answer was mailed on November 15, 2005 in this case. Concurrent with the filing of this Petition, Applicants are filing a Reply Brief and a request for an Oral Hearing.

Appellants submit that a number of grounds of rejection set forth in the Examiner's Answer mailed on November 15, 2005 constitute new grounds of rejection. Appellants request that the grounds of rejection identified below and the six new references which are being cited in the Examiner's Answer in support of the grounds of rejection be designated new grounds of rejection. Appellants request a corrected Examiner's Answer which identifies the rejections as new grounds for rejection. Appellants further request that prosecution be reopened.

The Examiner has raised six new references for the first time in the Examiner's response. They are:

- (1) Chen *et al.*; 2002, Molecular and Cellular Proteomics 1:304-313;
- (2) LaBaer; 2003, Nature Biotechnology 21:976-977;
- (3) Gygi *et al.*; 1999, Mol. Cell. Biol. 19:1720-1730;
- (4) Lian *et al.* 2001, Blood 98:513-524;
- (5) Fessler *et al.*, 2002, J. Biol. Chem. 277:31291-31302; and
- (6) Greenbaum *et al.*, 2003, Genome Biology 4:117.1-117.8.

These references were not previously cited in any of the prior rejections of record. Appellants submit that the citation of such new prior art references for the first time in an Examiner's answer constitutes a new ground of rejection and is not permissible.

Legal Analysis

The M.P.E.P. Section 1207.03 (III) states that:

A new prior art reference cited for the first time in an examiner's answer generally will constitute a new ground of rejection. If the citation of a new prior art reference is necessary to support a rejection, it must be included in the statement of rejection, which would be considered to introduce a new ground of rejection. Even if the prior art reference is cited to support the rejection in a minor capacity, it should be positively included in the statement of rejection. *In re Hoch*, 428 F.2d 1341, 1342 n.3, 166 USPQ 406, 407 n. 3 (CCPA 1970). However, where a newly cited reference is added merely as evidence of the prior well known statement made by the examiner, the citation of the reference in the examiner's answer would not constitute a new ground of rejection within the meaning of 37 CFR §1.192(a) (2). See also MPEP §2144.03.

The M.P.E.P. adds that:

In addition, if an Appellant has clearly set forth an argument in a previous reply during prosecution of the application and the Examiner has failed to address that argument, the Examiner would not be permitted to add a new ground of rejection in the Examiner's answer to respond to that argument but would be permitted to reopen prosecution, if appropriate. (Emphasis added; See M.P.E.P. §1207.03; Requirements for a new ground of rejection, II).

The Court of Customs and Patent Appeals considered this situation in *In re Hoch*, 428 F.2d 1341, 1342 n.3, 166 USPQ 406, 407 n. 3 (CCPA 1970). In that case there were two other references cited in the appeal which were not mentioned in the statement of either of the appealed rejections. The court held:

Appellant's complaint seems to be justified, and if we did not find the rejections based *solely* on Molotsky and the French patent to be sound, we might well feel constrained to reverse the decision of the board. Where a reference is relied on to support a rejection, whether or not in a "minor capacity" there would appear to be no excuse for not positively including the reference in the statement of rejection.

Appellants note that a Reply Brief must be in compliance with the requirements set forth in 37 C.F.R. §41.41. New or non-admitted affidavits and/or other evidence are not permitted in a reply brief.

For the detailed reasons set forth below, Appellants submit that the citation for the first time of these six references constitute a new ground of rejection and accordingly such rejections are not permissible.

Detailed Analysis

(1) Chen *et al.*; 2002, Molecular and Cellular Proteomics 1:304-313

The Examiner states at page 5, line 25 – page 6, line 8 of the Examiner's response that "Even if increased mRNA levels could be established for PRO269, it does not follow that polypeptide levels would also be amplified. Chen et al. (2002, Molecular and Cellular Proteomics 1:304-313) compared mRNA and protein expression for a cohort of genes in the same lung adenocarcinomas. Only 17% of 165 protein spots or 21% of the genes had a significant correlation between protein and mRNA expression levels. Chen et al. clearly state that 'the use of mRNA expression patterns by themselves, however, is insufficient for understanding the expression of protein products'(p.304) and 'it is not possible to predict overall protein expression levels based on average mRNA abundance in lung cancer samples' (pp.311-312)"

The Examiner makes reference to specific experimental details and statistical percentages present in the Chen reference for the first time. This constitutes a new ground of rejection.

The Examiner cites Chen throughout the Examiner's Answer, for example, in support of rejections at page 10, lines 10-14; page 11, lines 13-16; page 14, lines 12 -21; page 17, lines 19-22; page 18, line 19 – page 19, line 2; page 19, lines 12-14; page 20, lines 13 - 15; page 27, lines 4 - 12; page 28, lines 8-12; page 29, lines 17-20; page 31, lines 15-21; page 33, lines 11-16; page 35, lines 13-21; and page 40, lines 18-22.

Appellants submit that they are unable to adequately rebut the Chen reference and each of the rejections based on Chen without presenting substantive evidence of their own. The M.P.E.P. and the case law clearly state that the Examiner is not allowed to make new grounds of rejection and cite a new reference, Chen. Furthermore, it is inequitable to allow the Examiner to do so without allowing Appellants to present evidence in rebuttal. Appellants submit that the citation of Chen and raising of the grounds of rejection based on Chen constitute new grounds of rejection.

(2) LaBaer; 2003, Nature Biotechnology 21:976-977

The Examiner cites LaBaer for the first time on page 6, lines 16 - 20; where she states that:

“One of the authors of this paper, Dr. LaBaer made an even stronger statement that reports of mRNA or protein changes of as little as two fold are not uncommon, and although changes of this magnitude may turn out to be important, most are attributable to disease-independent differences between the samples.”

The Examiner cites LaBaer throughout the Examiner's Answer, for example, in support of rejections at page 10, lines 10-14; page 11, lines 13-16; page 15, lines 7-11; page 17, lines 19-22; page 18, line 19 – page 19, line 2; page 19, lines 12-14; page 20, lines 18-22; page 27, lines 4 - 12; page 29, lines 17-20; page 33, lines 11-16; page 36, lines 7 – 11 and page 40, lines 18-22.

In this case, the Examiner's basis for rejection that differences of as little as two fold are not uncommon and that changes of this magnitude relate to disease-independent differences between the samples” is being made for the first time.

Appellants submit that they are unable to adequately rebut the LaBaer reference and each of the rejections based on LaBaer without presenting substantive evidence of their own. The M.P.E.P. and the case law clearly state that the Examiner is not allowed to make new grounds of rejection and cite a new reference, LaBaer. Furthermore, it is inequitable to allow the Examiner to do so without allowing Appellants to present evidence in rebuttal. Appellants submit that the citation of LaBaer and raising of the grounds of rejection based on LaBaer constitute new grounds of rejection.

- (3) Gygi *et al.*; 1999, Mol. Cell. Biol. 19:1720-1730;
- (4) Lian *et al.* 2001, Blood 98:513-524; and
- (5) Fessler *et al.*, 2002, J. Biol. Chem. 277:31291-31302.

Similarly, regarding (3) Gygi, (4) Lian, and (5) Fessler, the Examiner cites these references for the first time in the Examiner's Answer on page 7. The Examiner states that Gygi *et al.* "conducted a similar study with over 150 polypeptides," Lian *et al.* "show a similar lack of correlation in mammalian (mouse) cells," and Fessler *et al.* "found a '[p]oor concordance between mRNA transcript and protein expression changes' in human cells". These references are presented for the first time and hence, each constitutes a new ground of rejection.

These references are further cited throughout the Examiner's Answer in support of various rejections, for example, at page 10, lines 10-14; page 11, lines 13-16; page 15, line 19 – page 16, line 14; page 17, lines 19-22; page 18, line 19 – page 19, line 2; page 19, lines 12-14; page 20, line 22 – page 21, line 5; page 27, lines 4 - 12; page 28, lines 8 – 12; page 29, lines 17-20; page 33, lines 11-16; page 36, line 19 – page 37, line 5 and page 40, lines 18-22.

Appellants submit that they are unable to adequately rebut these references and each of the rejections based on these references without presenting substantive evidence of their own. The M.P.E.P. and the case law clearly state that the Examiner is not allowed to make new grounds of rejection and cite a new reference. Furthermore, it is inequitable to allow the Examiner to do so without allowing Appellants to present evidence in rebuttal. Appellants submit that the citation of these references and raising of the grounds of rejection based on these references constitute new grounds of rejection. Appellants further request that prosecution be reopened.

- (6) Greenbaum *et al.*, 2003, Genome Biology 4:117.1-117.8.

Similarly, regarding (6) Greenbaum *et al.*, the Examiner cites this reference for the first time in the Examiner's Answer on pages 7 through 8. The Examiner states that Greenbaum *et al.*

"cautions against assuming that mRNA levels are generally correlative of protein levels. The reference teaches (p-age 117.3 2nd column) that primarily because of a limited ability to measure protein abundances, researchers have tried to find correlations between mRNA and the limited protein expression data, in the hope that they could determine protein abundance levels from the more copious and technically easier mRNA experiments. To date, however, there have been only a handful of efforts to find correlations between mRNA and protein expression levels, most notably in human cancers and yeast cells. And, for the most part, they have reported only minimal and/or limited correlations. The reference further teaches (page 117.4, 2nd column) that there are presumably at least three reasons for the poor correlations generally reported in the literature between the level of mRNA and the level of protein, and these may not be mutually exclusive. First, there are many complicated

and varied post-transcriptional mechanisms involved in turning mRNA into protein that are not yet sufficiently well defined to be able to compute protein concentrations from mRNA; second, proteins may differ substantially in their *in vivo* half lives; and/or third, there is a significant amount of error and noise in both protein and mRNA experiments that limit our ability to get a clear picture. The reference further notes (page 117.6, page 2nd column) that to be fully able to understand the relationship between mRNA and protein abundances, the dynamic processes involved in protein synthesis and degradation have to be better understood.”

This reference and each of these arguments are presented for the first time and hence, each constitutes a new ground of rejection.

This reference is further cited throughout the Examiner's Answer in support of various rejections, for example, at page 10, lines 10-14; page 11, lines 13-16; page 16, line 14 – page 17, line 8; page 17, lines 19-22; page 18, line 19 – page 19, line 2; page 19, lines 12-14; page 21, lines 5-9; page 27, lines 4 - 12; page 28, lines 8 – 12; page 33, lines 11-16; page 37, line 7 19 – page 38, line 2 and page 40, lines 18-22.

Appellants submit that they are unable to adequately rebut this reference and each of the rejections based on this reference without presenting substantive evidence of their own. The M.P.E.P. and the case law clearly state that the Examiner is not allowed to make new grounds of rejection and cite a new reference. Furthermore, it is inequitable to allow the Examiner to do so without allowing Appellants to present evidence in rebuttal. Appellants submit that the citation of these references and raising of the grounds of rejection based on these references constitute new grounds of rejection. Appellants further request that prosecution be reopened.

Appellants submit that this issue of the new grounds of rejections is being timely raised by the filing of this petition under 37 C.F.R. §1.181 with necessary fees and concurrently, with the filing of a Reply Brief within the two month period set for the Appellants' response.

Respectfully submitted,

Date: January 17, 2006

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